Structural and functional comparison of pyrrolnitrin- and iprodione-induced modifications in the class III histidine-kinase Bos1 of [i]Botrytis cinerea[/i]

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Structural and Functional Comparison of Pyrrolnitrin- and Iprodione-induced Modifications in the Class III histidine-kinase Bos1 of *Botrytis cinerea*

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Dicarboximides and phenylpyrroles are commonly used fungicides against plant pathogenic ascomycetes. Although their effect on fungal osmosensing systems has been shown in many studies, their modes-of-action still remain unclear. Laboratory- or field-mutants of fungi resistant to either or both fungicide categories generally harbour point mutations in the sensor histidine kinase of the osmotic signal transduction cascade. We compared the mechanisms of resistance to the dicarboximide iprodione and to pyrrolnitrin, a structural analogue of phenylpyrroles, in *Botrytis cinerea*. Pyrrolnitrin-induced mutants and iprodione-induced mutants of *B. cinerea* were produced *in vitro*. For the pyrrolnitrin-induced mutants, high level of resistance to pyrrolnitrin was associated with a high level of resistance to iprodione. For the iprodione-induced mutants, the high level of resistance to iprodione generated variable levels of resistance to pyrrolnitrin and phenylpyrroles. All selected mutants showed hypersensitivity to high osmolarity and regardless of their resistance levels to phenylpyrroles, they showed strongly reduced fitness parameters (sporulation, mycelial growth, aggressiveness on plants) compared to the parental phenotypes. The sequences of the osmosensing class III histidine kinase encoding gene *bos1* showed different mutations in both types of mutants. All of them affected the HAMP-domains of the histidine-kinase showing that each of the six HAMP domains is important for signal-transduction. Structure modelling of the HAMP domains revealed that the replacements of hydrophobic residues within the HAMP domains generally affected their helical structure, probably abolishing signal transduction. The mutation of residues E529, T581, or E692 – without consequences on HAMP structure – highlighted their involvement in signal transduction.